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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

ANDRES, JANET L

ART UNIT

PAPER NUMBER

1646

DATE MAILED: 02/11/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/605,266

**Applicant(s)**

AKELLA ET AL.

**Examiner**

Janet L Andres

**Art Unit**

1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 09 January 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-21, 23 and 24 is/are rejected.
- 7) ☒ Claim(s) 9-12 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election without traverse of PDGF in Paper No. 6 is acknowledged. Claims 1-24 are pending in this application. Claim 22 is withdrawn from consideration as drawn to non-elected species. The restriction requirement is made FINAL.

### ***Specification***

2. The use of the trademarks REGRANEX and XEROFORM has been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

### ***Claim Objections***

3. Claims 9-12 are objected to because they refer to a figure. Where possible, claims should be complete in themselves.

### ***Claim Rejections - 35 USC § 102***

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(c) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who

has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

5. Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. patent 5393739, Bentz et al., 1995. The '739 patent teaches a combination of a BMP and a TGF- $\beta$  in column 5, line 9. BMP-3 is specifically taught in line 13 and TGF- $\beta$  is specifically taught in line 16, thus anticipating claim 1. The '739 patent further teaches that the BMP component may contain mixtures of BMP-2, BMP-4, and BMP-7, anticipating the limitations of claim 2. TGF- $\beta$ 1 is taught in line 16, anticipating the limitations of claim 3. Factors purified from natural sources are taught in lines 18 and 19, anticipating claim 4. Synthetic and recombinant proteins and thus proteins free of histones are taught in lines 19 and 20. Applicant is reminded that a new use for a known composition does not render the composition novel. Further, fracture repair and repair of bone damaged by periodontal disease, taught in column 7, lines 34-36, are forms of wound healing.

6. Claims 1-8 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. patent 5459047, Wozney et al., 1995 and U.S. patent 5543394, Wozney et al., 1996. In column 2, line 48, the '047 patent teaches compositions of BMP-6 for wound repair and in lines 49-60 teaches that these compositions may also include BMP-2, BMP-3, BMP-5, and BMP-7, as well as FGF, TGF- $\beta$ , and PDGF. Therapeutic compositions and thus pharmaceutically acceptable carriers and purified proteins are taught in columns 7 and 8. The '394 patent teaches compositions of BMP-5 in a pharmaceutically acceptable carrier in column 2, lines 45-51 for use in bone or cartilage formation, wound repair, and tissue repair. Combinations with BMP-2, BMP-6, BMP-7, and FGF, TGF- $\beta$ , and PDGF are taught in lines 54-67 of column 2.

7. Claims 1-8 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. patent 6150328, Wang et al., filed June, 1991. In column 2, lines 25-53, the '328 patent teaches BMP-2 or BMP-4 for use in bone and cartilage formation as well as wound repair, and teaches combinations in a pharmaceutically acceptable vehicle containing BMP-3, BMP-5, BMP-6, BMP-7, FGF, and TGF- $\beta$ . Purification from bovine sources is taught in columns 7 and 8 and recombinant expression is taught in columns 14-17.

8. Claims 9-12 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. patent 5290763, Poser et al., 1994, U.S. patent 5563124, Damien et al., 1996, and U.S. patent 5371191, Poser et al., 1994. Figure 1 of each of these patents is identical to the instant Figure 1. Purified compositions in pharmaceutically acceptable carriers are taught in column 12 of the '763 patent and of the '191 patent and column 7 of the '124 patent.

***Claim Rejections - 35 USC § 103***

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 13-18, 20, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. patent 6150328 and further in view of U.S. patents 5393739 and 4950483, Ksander et al., 1990. The '328 patent teaches combinations of BMP-2, BMP-3, BMP-4, BMP-5, BMP-6, BMP-7, TGF- $\beta$ , EGF, and FGF for treatment of bone and cartilage defects, wound healing, and tissue repair in column 2, lines 34-65. The '328 patent does not teach the particular species FGF-1 or the species of TGF- $\beta$ , nor does it teach PDGF. FGF-1 (aFGF or acidic FGF) is taught by the '483 patent in column 2, lines 3-19. and PDGF is taught in line 8. The '483 patent does not teach the combinations set forth in the '328 patent. However, it would have been obvious to one of ordinary skill in the art to combine the teachings of the '483 patent and the '328 patent to use FGF-1 in the mixture taught by the '328 patent and to further add PDGF. One of ordinary skill would have been motivated to do so because the '483 patent teaches that PDGF and this species of FGF are useful components of a wound-healing mixture. The '483 patent further teaches that FGF is useful in combination with TGF- $\beta$  for wound healing (column 2, lines 9-13) but neither the '483 patent nor the '328 patent teach particular species of TGF- $\beta$ . TGFs- $\beta$ 1, 2, and 3 are taught in the '739 patent. The '739 patent fails to teach all of the components of the claimed combination. However, it would have been obvious to one of ordinary skill in the art to combine the teachings of the '739 patent with those of the '328 patent to use the different TGF- $\beta$  isoforms in the mixture taught in the '328 patent. One of ordinary skill would have been motivated to do so because the '739 teaches that these isoforms are members of the same family with the same effects on cell proliferation (column 3, lines 50-57).

11. Claims 19 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. patents 6150328, 5393739, and 4950483 as applied to claims 3-18, 20, and 23 above, and further in view of US patent 6124273, Drohan et al., filed October, 1997. The '328, '739, and '483 patents teach as set forth above but fail to teach hydrogels as in claim 19 or hydrogels or other dressings as claimed in claim 21. Hydrogels are taught by the '273 patent as delivery system for several of the claimed components, including FGF-1, PDGF, TGF- $\beta$ , and BMP-2 (column 16, lines 31-53). While the '273 patent fails to teach all of the components taught by the '328, '739, and '483 patents, it would have been obvious to one of ordinary skill in the art to combine the teachings of the '273 patent with those of the '328, '739, and '483 patents to use hydrogel to deliver all of the components of the claimed combination. One of ordinary skill would have been motivated to do so because the '273 patent teaches delivery of several of the components by this method, and further teaches hydrogel as an advantageous delivery system for growth factors in wound healing (column 3, lines 17-21 and column 16, lines 31-53).

12. Claim 24 is rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. patents 6150328, 5393739, and 4950483 as applied to claims 3-18, 20, and 23 above, and further in view of U.S. patent 5616490, Sullivan et al., 1997. The '328, '739, and '483 patents teach as set forth above but fail to teach inflammation inhibitors. Inhibition of TNF- $\alpha$  is taught by the '490 patent as a means to inhibit inflammatory disease (see the whole document). The '490 patent fails to teach inhibition of TNF- $\alpha$  in combination with growth factors to promote wound healing. However, it would have obvious to one of ordinary skill in the art to combine the teachings of the '490 patent with those of the '328, '739, and '483 patents to arrive at the method of claim 24. One of ordinary skill would have been motivated to do so because the '490 patent teaches that

the inflammation is an early step in wound healing, involving TNF- $\alpha$ , interleukin-1, and interleukin-6, and that these molecules can have deleterious effects (column 1, lines 17-56).

***Claim Rejections - 35 USC § 112***

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 9-13 and 16-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9-12 are indefinite in the recitation of "the histones"; there is no antecedent basis for this phrase.

Claims 10-12 is similarly indefinite in the recitation of "the ribosomal proteins".

Claims 9-12 are indefinite in the reference to "proteins as identified in Figure 1". No proteins are identified in Figure 1. Only bands on a gel are presented.

Claim 13 is indefinite in the repetition of "TGF- $\beta$ 2".

Claims 16 and 17 lack an antecedent basis for "the components".

Claim 18 refers to "claims 13". There is only one claim 13.

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Andres, Ph.D., whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.




If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564. The fax phone number for this group is (703) 872-9306 or (703) 872-9307 for after final communications.

Communications via internet mail regarding this application, other than those under U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

All Internet email communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Janet Andres, Ph.D.  
February 5, 2002

  
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